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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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COZEN O ' CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,495	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-148* is/are pending in the application.

4a) Of the above claim(s) *1-104 and 110-148* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105-109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Formal Matters

A. The Amendment dated 2/2/04 has been entered into the record.

B. Claims 1-148 are pending in this application. Claims 1-104 and 110-148 have been withdrawn as being drawn to a non-elected invention. Therefore, claims 105-109 are the subject of this Office Action.

C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Specification

A. The objection to the specification has been withdrawn in view of Applicants' amendment to the title to more closely reflect the elected subject matter.

3. Claim Objections

A. The objection to claims 105-109 has been withdrawn in view of Applicants' amendments to the claims to remove non-elected subject matter. The recitation of SEQ ID NO:115 is acceptable in the claims since it encodes SEQ ID NO:116.

B. Claims 105-109 are objected to since claim 105 recites "SEQ ID NO:116 SEQ ID NO:116." One recitation of "SEQ ID NO:116" should be removed. Claims 106-109 are objected to since they depend from claim 105.

C. Claims 105-109 are objected to since the syntax could be improved. As written, claim 105 is wordy. The claim could be rewritten, for example:

> An isolated polypeptide encoding a serotonin receptor where in said polypeptide has at least 95% sequence homology to SEQ ID NO:116 and encoded by a nucleic acid molecule having at least 95% sequence homology to SEQ ID NO:115.

It is brought to Applicants' attention that this claim suggestion is only acceptable if Applicants can demonstrate that the claim, as recited in the amendment dated 2/2/04, does not contain new matter, as discussed below in the rejection of claims 105-109 under 35 USC 112, first paragraph. It is also brought to Applicants' attention that the functional limitation of "encoding a serotonin receptor" is not appropriate as seen in the below scope rejection under 35 USC 112, first paragraph regarding this phrase unless Applicants provide persuasive arguments to that effect. The above example by the Examiner is only provided to demonstrate claim language with improved syntax as compared to present claim 105, but the Examiner's suggestions, themselves, will not overcome any rejections under 35 USC 112, first paragraph.

D. Claim 108 is objected to since it depends from claim 105, which has been rejected under 35 USC 112, first paragraph, as containing new matter. Claim 108 is not *rejected* since it recites the full-length protein of SEQ ID NO:116 and support for the limitation that the protein must be encoded by a nucleic acid molecule having at least 95% sequence homology to SEQ ID NO:115 is found on page 13, paragraph [00050] of the specification.

4. Claim Rejections - 35 USC § 101

A. The rejection of claims 105-109 under 35 USC 101 has been withdrawn in view of Applicants' arguments which state that the receptor of the present invention is a serotonin 5-HT_3 receptor. Based on a BLAST alignment, as provided in Applicants' present response, SEQ ID NO:116 exhibited 99% sequence identity with a known 5-HT_3 receptor. They argue that since the claimed polypeptide shares 99% sequence homology with a known serotonin receptor with a known function, this supports the assignment of the same specific, substantial, and credible utilities of the claimed polypeptides. Further persuasive are Applicants' arguments that numerous commercially available serotonin receptor products are available. Though it appears that the receptor of the present invention has a slightly higher homology to 5-HT_3E than to 5-HT_3C, the subtype alleged in the specification, Applicants did correctly disclose the receptor of the present invention as a 5-HT_3 receptor subtype. The Examiner has read the relevant literature, including the review by Glennon et al. (see at least pages 19-21), as cited by Applicants, and it is clear from the prior art that serotonin 5-HT_3 receptors do have utility. Therefore, regardless of whether the receptor of the present invention is a 5-HT_3C or 5-HT_3E, it has still been determined to be a member of the 5-HT_3 subfamily. The Examiner was not able to find any literature demonstrating that a "C" or "E" version of

receptor would have a different utility than that expected for the 5-HT_3 subfamily of serotonin receptors in general.

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. The rejection of claims 105-109 under 35 USC 112, first paragraph, as cited on page 5 of the Office Action dated 8/1/03, has been withdrawn in view of the finding that the claimed invention is enabled because it has utility as argued previously.

B. The potential rejection of claims 105-109 under 35 USC 112, first paragraph, regarding "homologous," "at least one conservative amino acid substitution" and "at least a portion," as discussed on page 5 of the Office Action mailed 8/1/03, is not being made since Applicants have amended the claims to delete these terms.

C. The rejection of claim 108 under 35 USC 112, first paragraph, has been withdrawn in view of Applicants' amendment to the claim to delete the term "allelic variant."

D. Claims 105-109 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO:116, does not reasonably provide enablement for polypeptides which are "at least 95% identical" to SEQ ID NO:116 and "**encode a serotonin receptor,**" including serotonin receptors from species other than human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The breadth of the claims is excessive with regard to Applicants claiming all polypeptides which have 95% identity to SEQ ID NO:116 and which "encode a serotonin receptor." These proteins would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:116. Applicants have demonstrated that the receptor of the present invention belongs to the 5-HT_3 subfamily of human serotonin receptors. However, the limitation recited in claim 105

includes, in scope, any serotonin receptor from any subfamily, as well as from species other than human. Applicants provide no guidance or working examples of polypeptides other than that of the full-length of SEQ ID NO:116, nor do they provide a *function* of these proteins. According to the review by Glennon et al. (as cited by Applicants), different serotonin receptor subtypes have distinct functions. Therefore, based on Applicants' disclosure of the receptor of the present invention as a 5-HT_3 subtype, Applicants have only provided sufficient guidance for the artisan to identify members of this human receptor subfamily both structurally and functionally (see the references submitted by Applicants on 2/2/04), but have not provided sufficient guidance how to identify members of other serotonin receptor subfamilies, for example, 5-$HT_{1, 2}$, or $_4$ receptors. Based on the literature cited by Applicants, there is no teachings of what amino acids are required to maintain the biological activity of serotonin receptors which are not human 5-HT_3 members, nor is it predictable to one of ordinary skill in the art how to make a functional serotonin polypeptide which is not a member of the human 5-HT_3 subfamily.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all polypeptides which are at least 95% identical to SEQ ID NO:116, but which are not members of the human 5-HT_3 subfamily. There is also a lack of guidance and working examples of these polypeptides. Applicants have not provided sufficient guidance how to identify members of other serotonin receptor subfamilies, for example, 5-$HT_{1, 2}$, or $_4$ receptors, or for species other than human. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make a functional serotonin polypeptide which is at least 95% identical to SEQ ID NO:116 and is not a member of the human 5-HT_3 subfamily, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. The rejection of claims 105-109 under 35 USC 112, first paragraph, regarding "homologous," "at least one conservative amino acid substitution" and "at least a portion" has been withdrawn in view of Applicants' amendments to the claims to delete these terms.

B. The rejection of claim 108 under 35 USC 112, first paragraph, has been withdrawn in view of Applicants' amendment to the claim to delete the term "allelic variant."

C. Claims 105-109 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Polypeptides having "at least 95% sequence homology" to SEQ ID NO:116 would have one or more amino acid substitutions, deletions, insertions and/or additions to the human protein encoded for by SEQ ID NO:116. Applicants have demonstrated that the receptor of the present invention belongs to the 5-HT_3 subfamily of serotonin receptors. However, the limitation recited in claim 105 includes, in scope, any serotonin receptor from any subfamily, as well as from species other than human. Furthremore, there is no functional language which will identify the serotonin receptors encompassed by the present claims as 5-HT_3 receptors such as, for example, rank order of affinity or binding a 5-HT3-specific ligand. **Though Applicants must keep in mind that the functional limitation cannot add new matter**. The Examiner suggested this language as an example only. Due to the length of the specification, the Examiner was unable to find exact language suitable for the present claims.

To continue, the specification and claims do not indicate what distinguishing attributes are shared by the members of the genus, which would include serotonin receptors other than those of the 5-HT_3 subfamliy. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. SEQ ID NO:116 is 471 residues in length and the claims allow for the alteration of up to 23 amino acids. The specification and claims do not provide any guidance as to what changes should be made, or where in the molecule these changes should be made in order to maintain a functional serotonin receptor; more importantly a 5-HT_3 receptor. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The fact that the claims limit the invention to molecules which encode serotonin receptors does still not adequately define the genus, as the specification only discloses one such protein, SEQ ID NO:116. Furthermore, this limitation does not differentiate the claimed invention, 5-HT_3 receptors, from other, undescribed, serotonin receptors such as 5-$HT_{1, 2}$ and $_4$. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "SEQ ID NO:116," alone, is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. No other species are described,

or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical amino acid residues which would structurally characterize the genus of serotonin receptors claimed, because it is unknown and not described what structurally constitutes any different amino acids encoding serotonin receptors from any species other than human; thereby not meeting the written description requirement under 35 USC 112, first paragraph. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

7. Claim Rejections - 35 USC § 112, first paragraph – new matter

A. Claims 105-107 and 109 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 105 now recites that the protein must have at least 95% sequence homology to SEQ ID NO:116 and must be encoded by a nucleic acid molecule having at least 95% sequence homology to SEQ ID NO:115. The only support for percent homology was found on page 13 of the specification (paragraph [00050]). The Examiner could not find support for "95% sequence homology" to the protein of SEQ ID NO:116, nor for the combination of percent homology for both the protein and nucleic acid. Furthermore, no support was found for the limitations in claims 106 and 107 regarding "98%" and "99% sequence homology", respectively. Applicants are required to point out exactly where in the specification support for these limitations can be found.

8. Claim Rejections - 35 USC § 112, second paragraph

A. All rejections under 35 USC 112, second paragraph, have been withdrawn in view of Applicants' incorporation of the desired limitations from claim 75 into the elected claims. Claim 75 has been withdrawn from consideration as being drawn to a non-elected invention.

9. Claim Rejections - 35 USC § 102

A. The rejection of claims 106 and 107 under 35 USC 102(b) as being anticipated by Dubin et al. has been withdrawn in view of the fact that the protein of Dubin is not at least 95% homologous to SEQ ID NO:116, as recited in independent claim 105.

B. Claim 106 remains rejected under 35 USC(e) as being anticipated by Wood et al. Claim 105 is now included in this rejection. However, the rejection of claim 107 over Wood is withdrawn in view of Applicants' amendment to recite that the protein must be at least 99% identical to SEQ ID NO:116. The protein of Wood is 97.8% identical to SEQ ID NO:116. However, to be consistent with claim 106 regarding the number of significant figures, "97.8%" rounded to "98%". Therefore, the protein of Wood meets the limitations of claims 105 and 106. This rejection is being maintained for claim 106 and made for claim 105. The fact that Wood do not teach a nucleotide sequence which has at least 95% homology to SEQ ID NO:115 is, respectfully, irrelevant. The claim is drawn to the protein. The nucleic acid molecule can be viewed as a "product-by-process" claim. The product (protein) is identical regardless of the "process" by which it is made (nucleotide sequence). One of ordinary skill in the art would not be able to differentiate the protein of Wood from that of the present invention simply due to a difference in nucleotide sequence.

Applicants argue that, since the present invention and the invention of Wood et al. were commonly assigned to Pharmacia & Upjohn Co. at the time of the present invention and that the present application was filed after November 29, 1999, the Wood patent publication would be disqualified as prior art under 35 USC 102(e)/103 or 103. This argument has been considered, but is not deemed persuasive. MPEP 706.02(l)(2) states that "...prior art under former 35 USC 103 via 35 USC 102(e) is now disqualified as prior art against the claimed invention if that subject matter and the claimed invention were [commonly owned]." However, this section of the MPEP further states that "Subject matter that qualifies as anticipatory under 35 USC 102(e), is not affected, and may still be used to reject claims as being anticipated."

The present invention claims benefit to numerous provisional applications. However, the present invention does not receive benefit to these applications since the newly amended claims (see 35 USC 112, first paragraph – new matter rejection) do not have support in these parent applications. If the new matter issue is resolved, then the present invention may find support in a parent (i.e. provisional) application.

10. Conclusion

A. No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
June 09, 2004

ROBERT LANDSMAN
PATENT EXAMINER